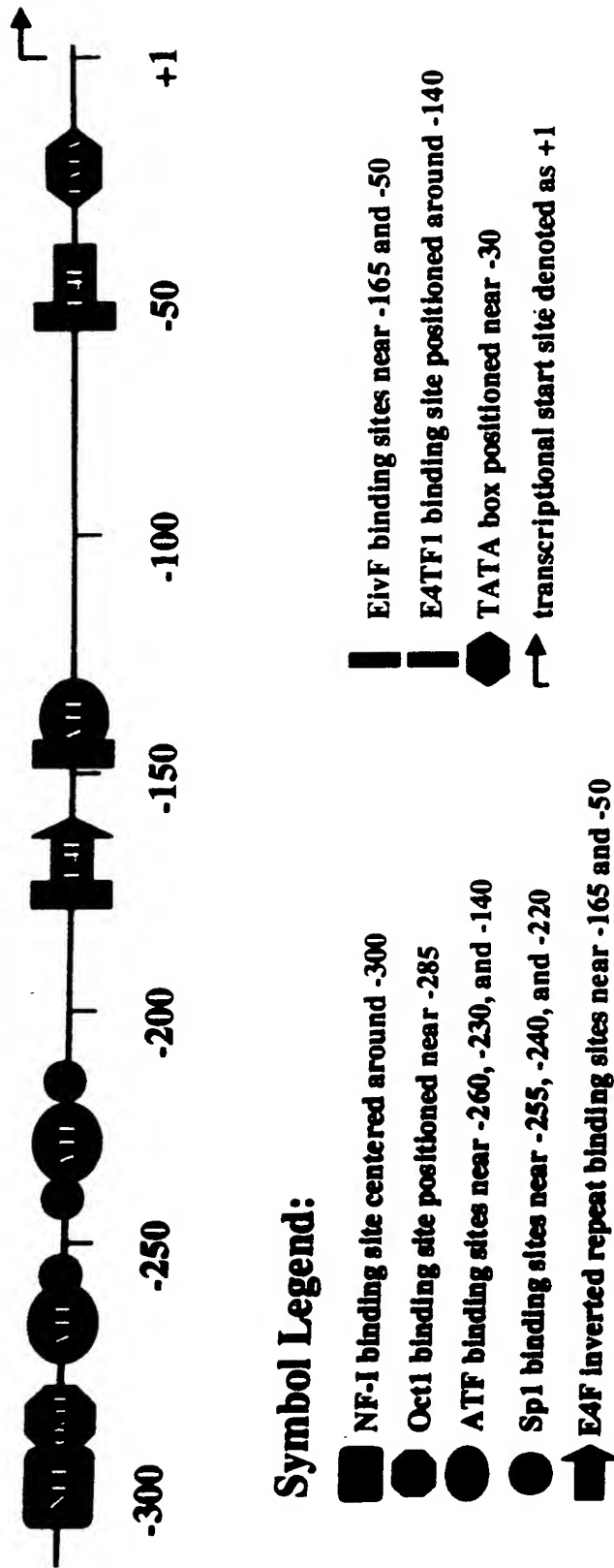


FIGURE 1



Symbol Legend:










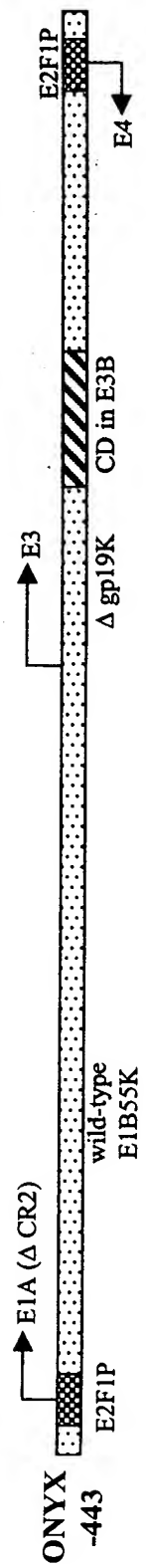
-  NF-1 binding site centered around -300
-  Oct1 binding site positioned near -285
-  ATF binding sites near -260, -230, and -140
-  Sp1 binding sites near -255, -240, and -220
-  E4F inverted repeat binding sites near -165 and -50
-  EivF binding sites near -165 and -50
-  E4TF1 binding site positioned around -140
-  TATA box positioned near -30
-  transcriptional start site denoted as +1

FIGURE 2

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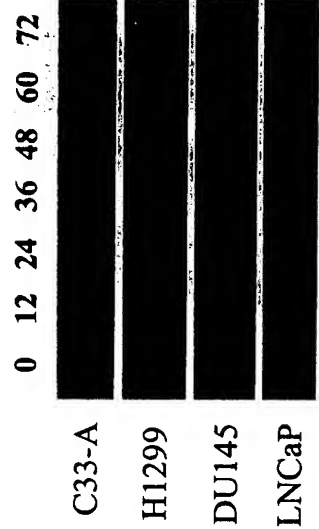
Figure 4.

A.



B.

Onyx 443

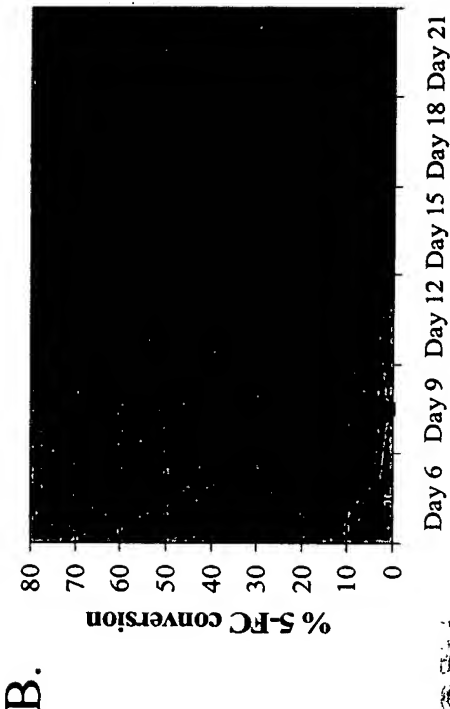
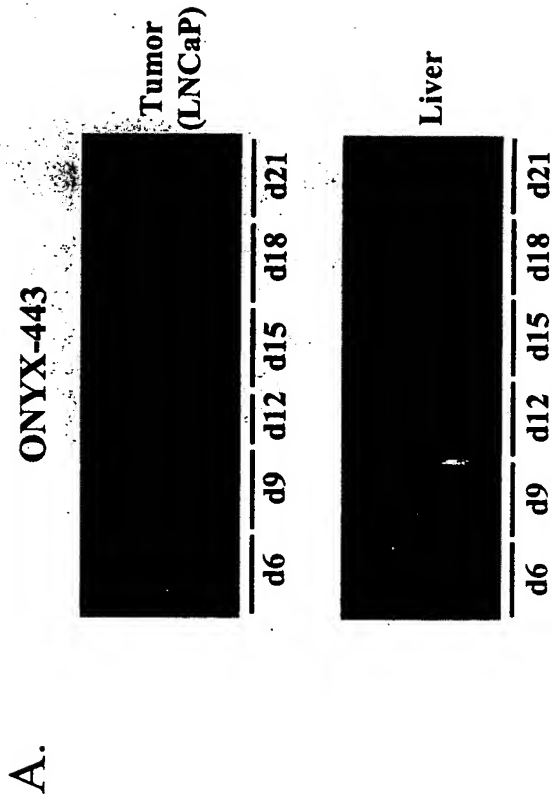


0 12 24 36 48 72

Hepatocytes

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Figure 5.



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Figure 6.

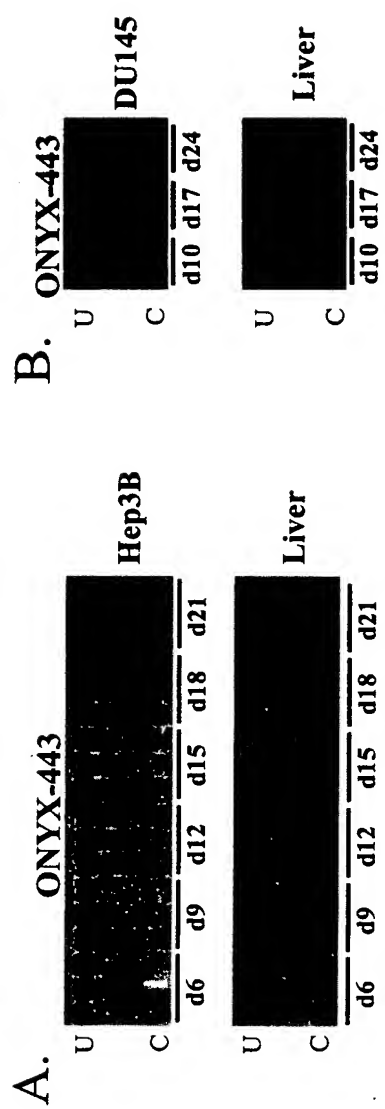


Figure 7. Genomic changes in ONYX-4XX. ITR: inverted terminal repeat; ψ : Viral packaging sequence; E2F1P: E2F1 promoter; H: Hind III site; B: BamH I site; X: Xho I site; S: Spe I site.

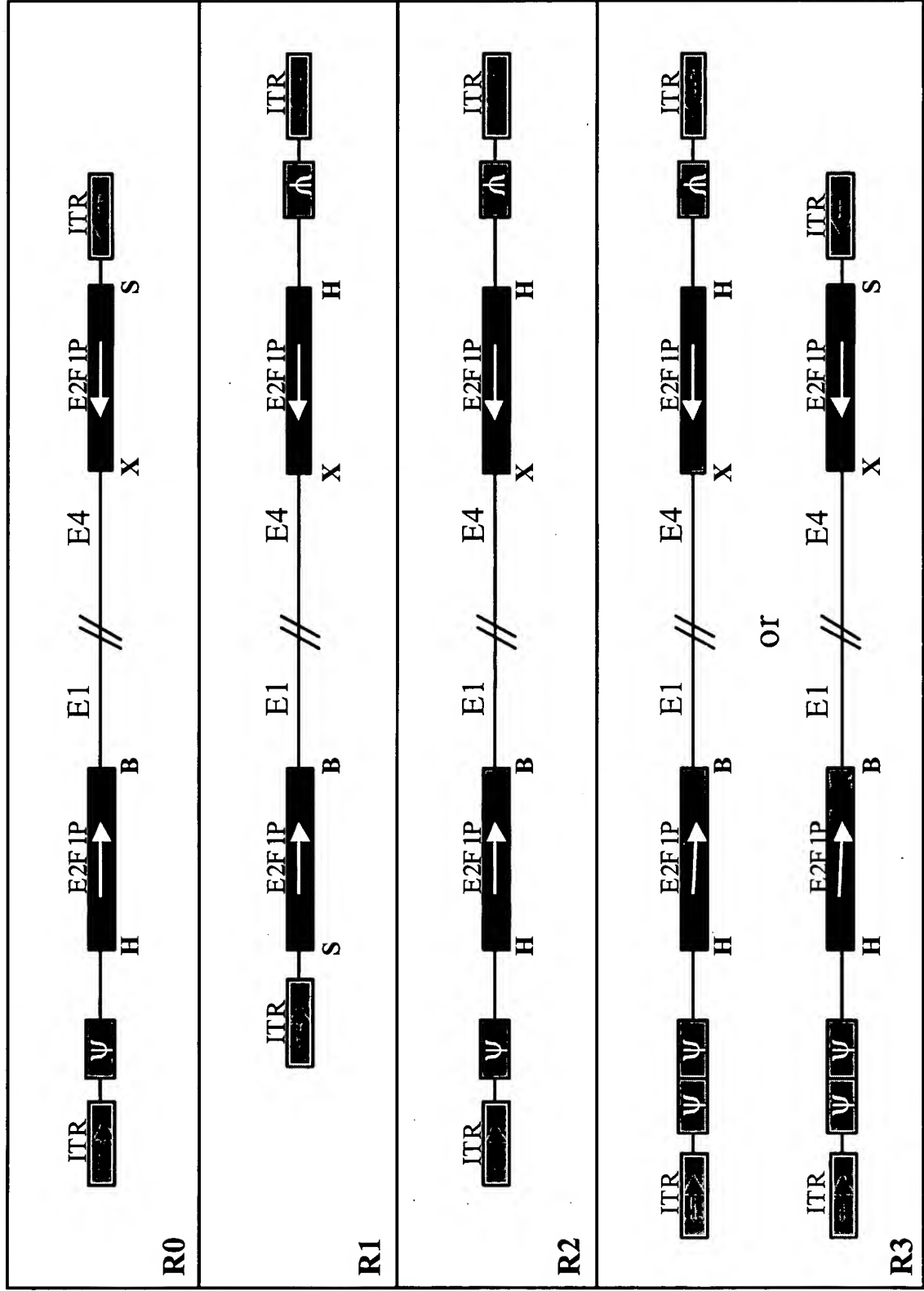
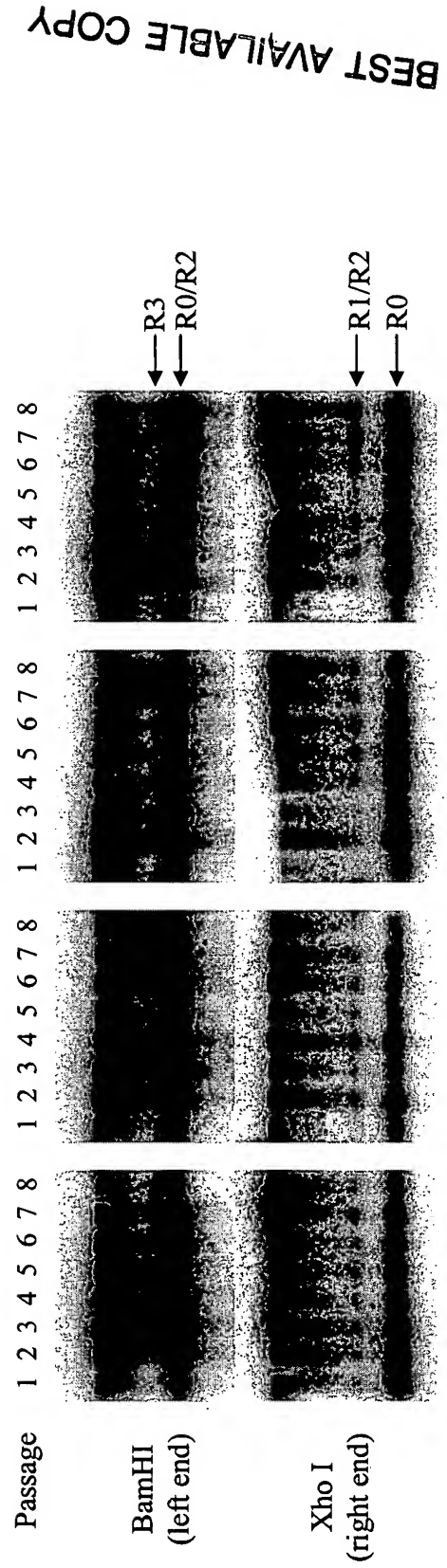
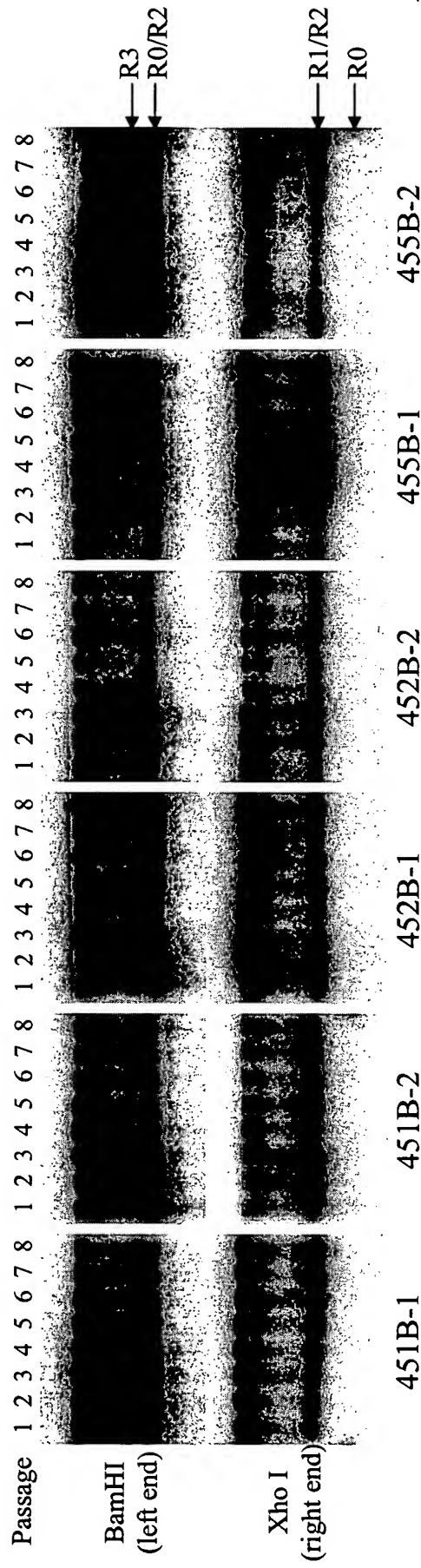


Figure 8. Sequencing Confirmation of ONYX-4XX R2 Termini

| | | | | | | | | | |
|-----|--|-----|-----|-----|-----|-----|-----|-----|------------------------|
| 1 | 10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 | Wild type ad5 left end |
| 1 | CATCATCAATAATATACCTTAATTTGGATTGAAGCCCAATATGATATAGGGGGTGGAGTTTGTGACGTGGCGGGGGCG | | | | | | | | ONYX-4XX-R2 left end |
| 1 | CATCATCAATAATATACCTTAATTTGGATTGAAGCCCAATATGATATAGGGGGTGGAGTTTGTGACGTGGCGGGGGCG | | | | | | | | ONYX-4XX-R2 right end |
| 81 | 90 | 100 | 110 | 120 | 130 | 140 | 150 | 160 | Wild type ad5 left end |
| 65 | TGGGAAACGGGGCGGGTGAAGTGTAGTGTGGCGGAAGTGTGATGTGGCACTGTGGGGAACACATGTAAAGCCACCGATG | | | | | | | | ONYX-4XX-R2 left end |
| 65 | TGGGAAACGGGGCGGGTGAAGTGTAGTGTGGCGGAAGTGTGATGTGGCACTGTGGGGAACACATGTAAAGCCACCGATG | | | | | | | | ONYX-4XX-R2 right end |
| 161 | 170 | 180 | 190 | 200 | 210 | 220 | 230 | 240 | Wild type ad5 left end |
| 145 | TGGCAAAAGTGAACGTTTGTGGTGTGGCGGGTGTACACAGGAAGTGAACAATTTTCGGCGGTTTTCGGCGGATGTGTGTAG | | | | | | | | ONYX-4XX-R2 left end |
| 145 | TGGCAAAAGTGAACGTTTGTGGTGTGGCGGGTGTACACAGGAAGTGAACAATTTTCGGCGGTTTTCGGCGGATGTGTGTAG | | | | | | | | ONYX-4XX-R2 right end |
| 241 | 250 | 260 | 270 | 280 | 290 | 300 | 310 | 320 | Wild type ad5 left end |
| 225 | TAAATTTGGGGCGTAAACCGAGTAAGATTGGCCCAATTTTCGGGGGAAACTCTGAATAAGAGGAAGTGAATACTCTGAATAATTTT | | | | | | | | ONYX-4XX-R2 left end |
| 225 | TAAATTTGGGGCGTAAACCGAGTAAGATTGGCCCAATTTTCGGGGGAAACTCTGAATAAGAGGAAGTGAATACTCTGAATAATTTT | | | | | | | | ONYX-4XX-R2 right end |
| 321 | 330 | 340 | 350 | 360 | 370 | 380 | 390 | 400 | Wild type ad5 left end |
| 305 | GTGTTACTCATAGCGCGTAATATTGTCTAGGGCGCGGGGACTTTTGACCGTTTACGTGGAGACTCGCCAGGTGTTTTT | | | | | | | | ONYX-4XX-R2 left end |
| 305 | GTGTTACTCATAGCGCGTAATATTGTCTAGGGCGCGGGGACTTTTGACCGTTTACGTGGAGACTCGCCAGGTGTTTTT | | | | | | | | ONYX-4XX-R2 right end |

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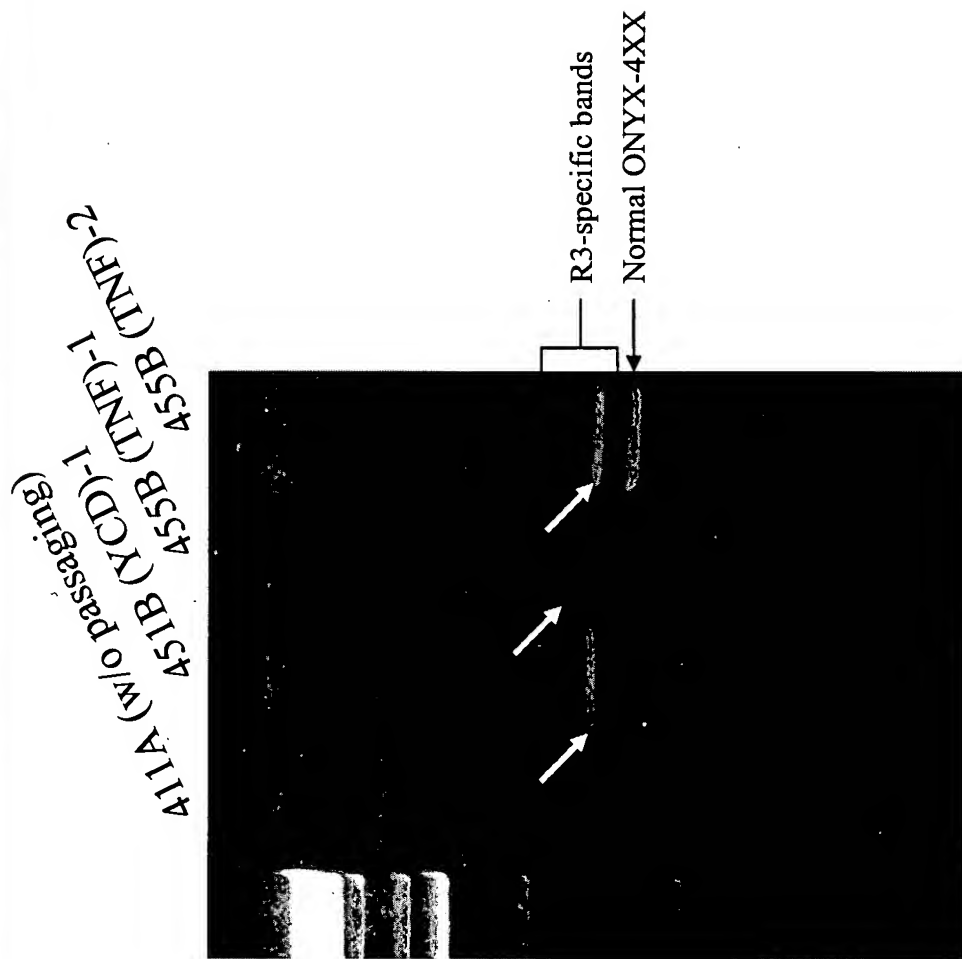
Figure 9 Southern Analysis of Viruses from Serial Passaging



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Figure 10. PCR Analysis of New Species



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Figure 11. Duplication of Packaging Sequence

1 -----GTGTAGTAAATTTCGG 107 bp YCD1.SEQ
1 -----TGTGTAGTAAATTTCGG 115 bp TNF2.SEQ
1 GAGTTTTTGGTGGCGGTTGACAGCAAGTGCACAATTTTGGCGGGTTTAGCGCGATGTTGAGTAAATTTCGG 202 bp TNF1.SEQ
1 -----GGTGTACACAGCAAGTGCACAATTTTGGCGGGTTTAGCGCGATGTTGAGTAAATTTCGG Ad5 packaging seq

AI

18 CGTAACCGAGTAAGATTTCGCCAATTTTCGGCGGAAACTCGAATAAGAGCAAGTGAATCTGAATAATTTCGTTACICA 107 bp YCD1.SEQ
19 CGTAACCGAGTAAGATTTCGCCAATTTTCGGCGGAAACTCGAATAAGAGCAAGTGAATCTGAATAATTTCGTTACICA 115 bp TNF2.SEQ
81 CGTAACCGAGTAAGATTTCGCCAATTTTCGGCGGAAACTCGAATAAGAGCAAGTGAATCTGAATAATTTCGTTACICA 202 bp TNF1.SEQ
62 CGTAACCGAGTAAGATTTCGCCAATTTTCGGCGGAAACTCGAATAAGAGCAAGTGAATCTGAATAATTTCGTTACICA Ad5 packaging seq

AII

AIII

AIV

98 TAGCGCGGTAA
99 TAGCGCGTAATATTGT
161 TAGCGCGTAATATTGTCTAGGCGCGCGGCGGACATTGACCGT
142 TAGCGCGTAATATTTCGTTAGGCGCGCGCGCGGCGGACATTGACCGT
107 bp YCD1.SEQ
115 bp TNF2.SEQ
202 bp TNF1.SEQ
Ad5 packaging seq

AV

AVI

AVII

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